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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/774,278	01/30/2001	Gregory M. Lanza	4375-000004/US	2535

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EXAMINER

SHARAREH, SHAHNAM J

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 02/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/774,278

Applicant(s)

LANZA ET AL.

Examiner

Shahnam Sharareh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11/4/02, 1/30/01.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3,5,13-19,25,26,31-35 and 68-71 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3,5,13-19,25,26,31-35 and 68-71 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

Applicant's election of Group I in Paper No. 9B is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant's election of the species of ligand, which is at least a portion of an antibody as, set forth in claims 69-71 is also acknowledged. Accordingly, the search is directed to such species.

Claims 1,3,7,8,13-19, 25-26, 31-35, 68-71 are pending in this application.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,3, 7,8,13-19, 25-26, 31-35, 68-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The limitation "ultrasound target" and the phrase "which binds to target" in claim 1 renders the claim ambiguous. First, it is not clear what an ultrasound target means? The specification further does not clarify this term accordingly. Second, the antecedent of the phrase "which binds to target" is not clear. Specifically, what is bound to the target, the emulsion, the liquid fluorocarbon or the nanoparticles therein? Accordingly, the metes and bounds of the claim are not clear.

While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161

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F.2d 367, 73 USPQ 482 (CCPA 1947). The term "the bound emulsion" in claims 1, 18, 19 is used by the claim to either mean "the liquid fluorocarbon," or "the nanoparticle," while the accepted meaning is "a colloidal dispersion of one liquid in another, immiscible or partially miscible, liquid." (see definition of "emulsion," page 152, Stensh, Dictionary of Biochemistry and Molecular Biology, 2nd ed.). Specifically, it is not clear how a colloidal dispersion as a whole may be in bound form.

Claims 1, 18, 19 recite the limitation "the bound emulsion." There is insufficient antecedent basis for this limitation in the claim. It is not clear to which bound emulsion is applicant referring?

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 8, 13, 18, 25-26, 31-35, 68-71 are rejected under 35 U.S.C. 102(b) as being anticipated by Milbrath US Patent 5,401,634.

The instant claims are directed to methods of changing acoustic reflectivity of a target comprising administering to the target a nongaseous emulsion comprising nanoparticle comprising liquid fluorocarbon, changing the temperature of the emulsion at the target site.

Mailbrath disclose the use of fluorochemical emulsions comprising a fluorochemical droplet having at least one specific binding species immobilized on the

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flurochemical droplet which further can contain a surfactant (see abstract, col 6, lines 45-55; col 8, lines 25-40; col 9, lines 18-47; col 14, lines 1-56; col 20, lines 64-69). The droplet size of Mailbrath's emulsion is in the range of 0.01micron (10 nanometer) to 500 microns (see col 7, lines 10-18; col 11, lines 43-57). Thus, Mailbrath's droplets meet the limitation of instant nanoparticles. Finally, Mailbrath discloses the step of detecting the droplets using short energy waves in the ragne of 610-612 nanometers which inherently causes local temperature change (see col 8, lines 25-29; col 17, lines 55-60).

Accordingly, Mailbrath meets the limitations of the instant claims.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

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were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1,3, 7-8,13-19, 25-26, 31-35, 68-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trevino et al US Patent 5,733,526 in view of Allen et al US Patent 5,527,528 and Unger et al US Patent 6,123,923.

Trevino teaches oil/flurochemical microemulsion systems wherein the emulsion comprise a bioactive agent, hydrocarbon oil particulates or droplets at least partially encapsulated in fluorochemical, and an emulsifying agent, wherein the fluorochemical is perfluorooctane (see abstract; col 8, lines 1-30, lines 60-64; col 9, lines 61-67; col 14, lines 52-67; col 17, line 60-col 18, line 10; col 19, lines 50-60). Trevino's compositions can be used as therapeutic and diagnostic agents using conventional methodologies (see col 13, line 60-col 14, line 15). The particle size of Treviono's microemulsion are very small in the ranges of less than 100 nm in diameter, thus, Trevino's microemulsion contain nanoparticles (col 18, lines 55-67, col 19, lines 116). Trevino fails to employ a targeting agent or explicitly use an energy source to measure the effects of his composition at a site of interest.

Allen is used solely to show that attaching a targeting agent such as an antibody molecule, to the surface of lipid vesicles is well established in the art employing various methodologies (abstract, col 12, lines 26-col 13, lines 5; also see example 1-3, for

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different methodologies). Allen's vesicles are larger than instant particles, specifically, Allen doesn't teach nanoparticles.

Unger teaches emulsion compositions for therapy or imaging comprising nanoparticles, fluorinated gaseous precursors such as perfluorooctane, and targeting ligands (see abstract, col 78, lines 46-60). The vesicle sizes of Unger's emulsion can be as small as 30 nm in diameter (see col 90, lines 57-col 91, line 30). Unger also teaches the use of external energy such as ultrasound or an optical resonating source to scan the site of interest (see col 121, lines 19-25; col 123, line 5; col 125, line 15-col 126, line 10). Unger fails to explicitly use perfluorooctane liquid in his compositions.

Nevertheless, it would have been obvious to one of ordinary skill in the art at the time of invention to link a targeting ligand to the nanoparticles of Trevino by well-known methods, as taught by Allen and Unger, and further employ an external source of energy as taught by Unger to detect the location of the administered nanoparticles at the site of interest. The ordinary skill in the art would have been motivated to do such modifications because as taught by Unger, he would have had a reasonable expectation to improve specificity of the imaging or therapeutic methodologies of choice.

### ***Conclusion***

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh, PharmD whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 703-308-1877. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

RUSSELL TRAVERS  
PRIMARY EXAMINER  
GROUP 1200

ss  
January 27, 2003